B A S A L N A R C O S I S

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With special reference to the use of

Tri-bromethanol (Avertin)

THESIS

-- for Degree of M.D. --

- by -

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BASAL NARCOSIS, with special reference to the use of Tri-brom-Ethanol (Avertin)

General Remarks

The production of general anaesthesia by means of the inhalation anaesthetics alone has many drawbacks in practice, which are appreciated by the patient, the surgeon and the anaesthetist.

The psychological effect on the patient of such a procedure is frequently so great that it is not too much to say that it may influence the whole prognosis of his case.

Any anaesthetist of experience knows that a nervous patient frequently takes the anaesthetic badly, having a stormy induction period, and requiring particularly careful supervision during the subsequent administration. In many instances, such a patient appears to have a heightened shock readiness. Whilst this is obvious in a nervous patient, there is in all patients some degree of apprehension prior to operation and any safe means of eliminating this psychological factor should be adopted.

From the purely operative point of view, the surgeon welcomes an anaesthetic which will give good muscular relaxation, whilst he dreads the common sequelae of the older anaesthetics: post-operative vomiting and lung

complications. It is also realised that the degree of surgical shock produced depends largely on the duration of the operation and the amount of anaesthetic used.

The perfect anaesthetic has yet to be discovered. The requirements of such an anaesthetic would be that it should give an easy and pleasant induction, that it should be non-toxic and non-shock-producing in ordinary doses, that it should give good muscular relaxation, that it should be easily and quickly eliminated from the system, that it should not be followed by vomiting and lung irritation, that it should be easily prepared, requiring little apparatus for administration and that its cost should be reasonable.

In the opinion of the writer, Tribromethanol (hereinafter referred to as Avertin) is a marked advance on any previous drug in the direction of the perfect anaesthetic, and fulfils some of the requirements enumerated above. It cannot, however, be used as the sole anaesthetic agent and it is there that it just fails.

Basal Narcosis in general

"I believe that no patient should come to general or local anaesthesia for any serious operation without preliminary sedatives of the morphia type, or an adequate dose of one of the "basal anaesthetics" unless there are real contra-indications, of which however, there can be

but few." This statement made by Clausen[2] in a stimulating paper on the progress of anaesthesia, is indicative of the modern trend of thought and research in anaesthetics.

Prior to the introduction, within the last few years, of what are generally known as the Basal Narcotics, alleviation of the patient's apprehension was frequently brought about by the administration of premedicaments of the morphia type and this practice is still in common use where more modern methods have not yet been adopted.

The first successful attempts at producing basal narcosis without grave risk to the patient were those of Gwathmey, who in 1913 introduced his now well-known colonic oil-ether technique, which he later further developed into his synergistic method, using multiple drugs of different pharmacological properties in order to reinforce their action. It is interesting to note in this connection that, within five years of the discovery of the anaesthetic properties of ether, Pirogoff in 1847 suggested its use by the rectal route and this was tried by himself and other French workers, but the results of their technique were generally poor and did not justify the extra risks involved.[3]

Colonic oil-ether has never been so popular in this country as it has been in America, mainly owing to the risk of rectal irritation and to the amount of extra nursing involved.

Gwathmey's work, however, is the basis of most of the newer methods of rectal anaesthesia. Rowbotham[4] acknowledges his indebtedness to Gwathmey in the evolution of his own technique for the administration of rectal paraldehyde and the mode of employment of Avertin embodies many of Gwathmey's original ideas.

The drugs in general use at the present time as basal narcotics are paraldehyde, avertin and the barbiturates (sodium amytal, nembutal and pernocton). Since the introduction of Avertin, paraldehyde has almost dropped out of use. Paraldehyde and avertin are administered rectally, and the barbiturates are usually given intravenously, but nembutal may be given by the mouth.

The chief advantages gained by using basal narcotics are that they abolish apprehension on the part of the patient, they lessen the amount of inhalation anaesthetic required, they give a pleasant and peaceful induction, they give a period of post-operative sleep, they practically obviate post-operative vomiting, and it is generally believed that their use tends to obviate post-operative lung complications.

Scope of Thesis

In the following pages it is proposed to discuss Avertin as a basal narcotic giving details of its properties, technique of administration and scope. Observations will

be included as a result of a study of the literature pertaining to the subject and also as a result of personal experience of the use of the drug in a variety of different conditions.

AVERTIN (Tri-brom-ethyl-alcohol, E107)

Historical: In 1923 Willstaetter and Duisberg produced tri-brom-ethyl-alcohol in Germany. Its use as a rectal anaesthetic was first suggested by Professor Eicholtz in Berlin and in March 1926 Butzengeiger first used it clinically.

The initial results were extremely satisfactory and in view of this it says much for its sponsors that it was only after an elaborate and extensive trial had been made under all conditions that the drug was issued to the profession for general use.

Avertin first came on the general market in 1929, backed by the records of thousands of cases made by reliable authorities, and has thus suffered less from hasty and ill-considered publicity than many new preparations have done in the past. It was early decided that its proper use was as a basal narcotic, and not as a general anaesthetic as had been originally hoped.

Following thorough clinical trials in Germany, supplies were issued for trial in other countries. In Great Britain, Sir H.H. Dale, Director of the National Institute of Chemical Research had control of the supplies and distributed the drug to a number of well-known surgeons and anaesthetists chosen from the Anaesthetics Committee of the Royal Society of Medicine and the Medical Research Council. The reports of these observers were, on the whole, favorable (5,6,7).

During 1929 the drug was issued for general use and has since been used in all parts of the country under varying conditions. On the whole, the results have been satisfactory and the few accidents reported earlier can now be shown to have been due to faulty technique which has since been remedied.

With the passage of time and its continued and increasing use throughout Great Britain, Avertin may be said to be firmly established as probably the most generally applicable of all the basal narcotics.

Chemistry of Avertin

Avertin has the formula C Br_3CH_2OH and was originally produced by the fermentation of Bromal with yeast. It is now manufactured by a simpler process designed by Meerwein

and Nord. The dried product is a white crystalline powder melting at 79°c to 80°c. , It is easily sublimated and is volatilised by steam. As it is slightly affected by light it should be stored in a cool dry place and protected from light and atmospheric influences. The powder is soluble in water up to 3½% at body temperature. Even after exposure to this temperature for eight hours less than ·3% decomposes. At higher temperatures (from 40°c to 45°c) Avertin loses hydrobromic acid and becomes dibromvinyl alcohol, which alters to dibromacetaldehyde thus :-

$$CBr_3CH_2OH = CBr_2\ CHOH + HBr$$
$$CBr_2CHOH = CHBr_2\ CHO$$

This reaction is exceedingly important from the clinical point of view, as even the most minute traces of dibromacetaldehyde are very irritating to the bowel.[8]

To facilitate ease of preparation, Avertin is now supplied as "Avertin Fluid" - a clear, oily-looking, heavy liquid, with a strong fruity odour. Solution of the drug is facilitated by the addition of amylene hydrate. Morrin[7] says 1 c.c of Avertin fluid is more efficacious than 1 dram of solid avertin, the therapeutic equivalent being 1 c.c. fluid avertin equals 1·25 grams of solid avertin. He also holds that it produces better relaxation and has less depressant effect on the respiration and blood-pressure.

Fluid Avertin contains 1 gram of solid avertin dissolved in 1 c.c of amylene hydrate. The latter drug is said to have anaesthetic properties of its own and to be a respiratory stimulant.

Pharmacology of Avertin

Absorption: One of the striking clinical facts about Avertin administration is the rapidity with which the drug is absorbed by the bowel. It is difficult to find traces of the drug in a washout withdrawn even 20 minutes after administration.

Drugs administered by the rectum are of course dealt with by the portal system. The liver deals habitually with substances, toxic and otherwise, which are absorbed by the bowel. Avertin has thus to pass through the liver before exercising its effects on the central nervous system. This appears to be a great advantage which the rectal route possesses over the intravenous. It is known that toxic substances have much more effect on the liver substance when they reach it by the hepatic artery instead of by the portal vein. Substances arriving by the latter route are apparently detoxicated by the liver and in the case of rectal anaesthetics only the excess of the drug is allowed to pass into the systemic circulation. This liver control prevents the sudden effects produced by flooding the circulation with a toxic drug as in the

parenteral injection of anaesthetic substances, and probably makes for a greater margin of safety. Avertin is known to have a definite effect on the liver cells, somewhat akin to that seen in chloroform or phosphorus poisoning. According to the most recent research this effect has probably been over-estimated in the past[9]. The fact that the liver can suffer extensive damage without giving symptoms and that it has exceptional recuperative powers, also makes for safety.[10]

Excretion: Avertin, as already stated, is dealt with by the liver, combining with glycuronic acid, and is excreted almost entirely by the kidneys as glycuronates.[11]

Parsons (8) states that he could not determine the form in which Avertin was excreted but that it was probably an organic compound of bromine other than avertin or urobromalic acid.

Dixon in an early paper on the subject[12] says that avertin owes its action to the formation of sodium bromide and that excretion can be aided by giving 5 to 10 grams of common salt in suitable solution, to increase the blood chlorides. One has not seen any further mention of this in subsequent articles.

Parsons (8) states that 53% to 73% is excreted in the first 24 hours, and on the ground that 37% remains in the body advises against a subsequent administration

within 24 hours. That this precuation is not necessary clinically is evidenced by the successful use of as many as 3 doses per diem in a case of tetanus under Momburg and Rotthaus.(13) It is probable that the 37% mentioned by Parsons as remaining in the body is innocuous. Other workers question the accuracy of Parson's technique of estimating the excreted bromide.(14)

Detoxication: Extensive experiments on animals have been carried out to determine detoxication times for Avertin, but the lower animals detoxicate the drug far more rapidly than man, so that fair comparison is impossible.

Various mutilating procedures have been carried out on animals to ascertain whether or not they altered detoxication time. None of them had any marked effect except extirpation of both adrenals(15). One curious fact emerged, however, and that was that thyroidectomy made no difference to detoxication time, whereas the administration of thyroxin reduced the mortality in animals which had had average lethal doses, and also shortened the recovery time. When one takes into consideration the fact that from a ton of fresh gland only 270 grams of thyroxin can be obtained by Harington's method(16) this is not so surprising, as the amount of thyroxin in a single gland must be very small and in the experiments the amount used was

·3 to 1 gram unit of thyroxin per 200 grams of body-weight.

In the human subject various substances have been employed for detoxication purposes. Lobeline, ephedrine, cardiazol, sodium thiosulphate and coramine have all been used with effect. The two latter seem to be the most successful. Bolliger[17] has conducted animal experiments using sodium thiosulphate and concludes that lavage of the bowel with a 20% solution of this drug is of value in cases exhibiting alarming symptoms after avertin. Maddox[18] had an opportunity of testing the use of this drug on a child requiring repeated doses of avertin. He used 300 c.c. of a 20% solution about 50 minutes after the avertin administration but did not find any appreciable difference in recovery time compared with the times avertin was given alone. The experiment was, however, vitiated by the fact that the child developed a tolerance to avertin.

Kennedy[19] following the work of Killian has used coramine successfully (2 c.c. to 3 c.c. given intramuscularly) and considers that it also has advantages over CO_2 as a respiratory stimulant.

Ephedrine and Lobeline, both recommended for raising the blood pressure and as respiratory stimulants, may also act in part as antidotes (20) as also does the administration of a mixture of CO_2 and oxygen. Presumably

they act by increasing the basal metabolic rate, a factor which Lewis (21) regards as of great importance in dosage.

Desmarest[22] is enthusiastic about the combination of nitrous oxide and oxygen, not only as a supplementary anaesthetic, but as a raiser of a blood-pressure depressed by avertin.

Thyroxin is practically useless as a detoxicating agent in an emergency as it is slow-acting and has to be administered for some time before operation in order to have any effect.

Effects on the Cardio-vascular system : One of the most startling and immediate effects of the administration of avertin is the fall in blood-pressure which, in greater or in less degree, takes place in every case. According to Kennedy who has observed a large number of cases the fall varies from 2^{mm}. to 102^{mm} of mercury. Blomfield and Shipway[5] place the average fall at 10^{mm} of mercury. Maddox[23] has had experience of cases with falls of 30^{mm} to 40^{mm} of mercury where the difference could be appreciated by palpation of the radial pulse.

The earlier observers were inclined to lay much stress on this fall of blood-pressure, but clinical observation has shown that, in the vast majority of cases, it has no significance; in fact, the condition

of the patient is apparently very satisfactory even when a large fall has taken place. Young[24] states that he views the fall of blood-pressure in Avertin cases "with increasing equanimity" and Kennedy[19] after an experience of 1350 of Young's cases, re-affirms this view. Taylor and Lund[25] point out that the clinical state of the patient gives no indication of the depth of fall of blood-pressure, and give as the reason the fact that the ratio of pulse pressure to diastolic pressure remains unaltered. They also conclude that the alteration in pressure is independent of surgical shock.

The personal experience of the writer is in accord with the foregoing opinions as he has noted falls of up to 35^{mm} of mercury without any untoward clinical phenomena, and, as the readings were taken on the operating-table prior to the administration of the supplementary anaesthetic and to the commencement of the operation the question of surgical shock did not arise.

Means for combating a fall of blood-pressure causing anxiety have been mentioned in the section on detoxication. In addition, it may be mentioned that the mere administration of a little open ether is quite sufficient to raise the pressure in the average case.

Probably the fall of blood-pressure under avertin is much akin to that which takes place during normal sleep. The pulse-rate varies after avertin. In some

cases it is unaltered. In the majority there is a slight acceleration and occasionally this may be very marked, particularly in cases suffering from hyperthyroidism. As a rule, with the establishment of narcosis the pulse rate settles down, and it is only in the induction stage that the change is noticeable.

Hill (26) has shown that the electrocardiogram of patients anaesthetised with avertin is altered, thus demonstrating that the drug has some action on the heart muscle. The probability is that, owing to its chemical similarity to chloroform, its effects are similar, but in a much less degree. In any case no fatalities are recorded as being due to the action of the drug on the heart; effects on that organ only being seen after the respiratory system has been grossly affected.

Effects on the Respiratory System: Most observers are agreed that avertin has a definite depressant effect on the respiratory centre, and most of the deaths recorded are due to respiratory failure. A study of the recorded deaths shows that, in the majority of them, morphia was administered as a premedicament and there is no doubt that the combination of the two drugs, both of which depress the respiratory centre, must therefore be used with great care.

Usually, patients narcotized with avertin are not cyanosed and have slow, regular, shallow respiration akin to that seen in normal sleep.

The fact that avertin depresses respiration makes it more than usually important to maintain a free airway throughout the anaesthesia and to have respiratory stimulants at hand in case of need. Lobeline, ephedrine, coramine and CO_2 and oxygen are probably the most useful and have all been employed successfully.

Effects on the Central Nervous System: Avertin acts in a similar manner to other bromide compounds and its first and most marked effects are on the cells of the cortex. It is probable that, owing to its physical similarity to chloroform, avertin enters into combination with the lipoids of the cortical cells.

The higher centres of the brain are thus the first to be affected, and the lower centres last. There is a large margin of safety in normal doses, as detoxication takes place rapidly and the vital centres in the medulla are only slightly affected.

In contrast to the inhalation anaesthetics which are excreted rapidly by the lungs and whose anaesthetic effects are quickly lost on cessation of administration, avertin narcosis passes off slowly, and in the reverse order to its onset, the higher centres being the last to recover. This is the reason for one of the great

benefits of avertin narcosis, the quiet after-period.

Another very striking effect of avertin is the almost unfailing amnesia which it provides. Patients who may not be fully narcotised, and who may talk rationally up to the administration of the supplementary anaesthetic, never remember anything after the rectal injection. This amnesia is so remarkable that it has to be seen to be believed.

Scope of Avertin Narcosis

Avertin may be used with safety as a basal narcotic in practically every surgical condition, some medical conditions (for example tetanus and mental disease) and in obstetrics.

Most writers on the subject are agreed that it should not be used for operations in the region of the anus or rectum for obvious reasons and in the writer's opinion tonsillectomy under avertin (unless an elaborate technique is used) exposes the patient to unnecessary risks, though the anaesthesia produced is well-nigh perfect for the performance of the operation.

Certain Clinical Conditions where Avertin Narcosis is specially indicated

(1) Hyperthyroidism. In patients suffering from this condition where partial removal of the thyroid gland is indicated avertin is of the greatest possible use. Such persons must be protected as far as possible from psychological trauma and, owing to their increased metabolic rate, the drug is rapidly detoxicated and is therefore safe.

Crile's plan of "stealing the goitre" can be carried out with ease under avertin and the delight of the patients themselves on recovery is extremely gratifying.

Patients suffering from hyperthyroidism may require larger doses than normal. Lewis (21) and Edwards (27) say that in such cases the body weight is only useful as a rough guide to dosage and that the Basal metabolic rate is a more useful guide. They worked out the Basal metabolic rate according to Read's formula and found that it bore a definite relationship to the time which the patient took to succumb to the drug.

(2) Cardiac Cases: Avertin is probably safer than ether or chloroform alone in such cases. In the first place it is probably much less toxic than ether or chloroform in the dosage usually given, and in addition it obviates the period of struggling

and breath-holding so commonly seen during induction, especially with ether. The fact that the avertinized patient usually breathes evenly and regularly and thus keeps his vital centres well supplied with oxygen is of great benefit.

(3) Diabetic cases: Surgery in diabetes is always fraught with danger. The commonest methods of anaesthesia in use at present in diabetic subjects are - 1. Local anaesthesia, 2. Spinal anaesthesia (where applicable) and 3. Gas and oxygen, all preceded by suitable amounts of insulin and glucose.

Vomiting after operation in a diabetic is a very serious complication as it tends to increase the risk of acidosis, and it is common knowledge that diabetics are particularly liable to pulmonary complications.

Avertin, therefore, has been used in the surgery of diabetes with success as it reduces post-operative vomiting and when gas and oxygen is used as the supplementary anaesthetic, as it should be, the risk of pulmonary mischief is much reduced. Avertin has this advantage over local anaesthesia, that it does not interfere with the healing of tissues of already reduced vitality (28).

(4) Mental cases: In the surgery of the insane avertin is of great value in obviating the psychological factor and narcosis is usually much more simply induced by the

rectal method in maniacal cases than by inhalational means.

Contra-indications to the use of Avertin

As a result of recent research and further clinical experience many conditions which were originally thought to negative the exhibition of avertin are now being successfully treated in increasing numbers. Such conditions are: diseases of the liver and kidneys and certain degrees of thyroid deficiency. The reason for the alteration in point of view is that the action of the drug on the various organs concerned is now better understood and that the value of certain drugs, for example thyroxin and ephedrine, for previous or simultaneous administration is better appreciated. The continued successful use of the drug in cases which were at first thought to be entirely unsuitable adds valuable clinical evidence of the wider scope of avertin.

The contra-indications given by Hewer[29] seem to cover all contingencies and may be quoted: (1) Patients with very low metabolic rates (2) Patients who require a rapid return of reflexes after operation (3) Patients with an abnormally low blood pressure (one might also add patients with an abnormally high blood pressure)[30] (4) Patients who require the use of other methods or

drugs which tend further to lower the blood pressure: for example, high spinal blocks, (5) Patients who may require the use of drugs which will further depress the respiratory centre (6) Patients requiring operations on the rectum or anus (7) Patients suffering from very marked disease of the liver or kidneys, (this last must be qualified in view of clinical experience[31] and the most recent work of Parsons[9]. Also avertin has been used successfully in the treatment of eclampsia, and most cases of cholecystitis with hepatitis react normally to the drug[32]. Probably patients suffering from gall-bladder disease derive great benefit from avertin as the excellent relaxation of the abdominal muscles and the small respiratory excursion of the diaphragm greatly diminishes the difficulty of cholecystectomy and obviates handling and traction. Unilateral kidney disease is not a contra-indication to the use of avertin and many successful nephrectomies have been performed under it.

As the bulk of the drug is excreted by the kidneys nephritis of any marked degree must be a contraindication, but apparently, in whatever form the drug is excreted it is practically non-irritating. Bolliger and Maddox[33] after experiments on animals conclude that avertin can be safely administered to the human

subject suffering from mild or moderate degrees of renal insufficiency. Evidence on this point is, however, sufficiently doubtful to render one chary of using a drug which may possibly further prejudice the chances of a patient already in danger from renal disease, as the result of surgical procedures on kidney action cannot be gauged prior to operation. For this reason the writer has not used avertin in cases of prostatic disease requiring operation, but has preferred the use of spinal analgesia, preceded by oral nembutal and supplemented by gas and oxygen if necessary.

Relative Contra-indications

Patients debilitated by long illness or sepsis, cachectic patients, and those suffering from shock due to haemorrhage or otherwise, are probably better treated by means other than avertin, but if the drug is used in such cases, then it is advisable to reduce the dosage.

The very young and the very old are not as a rule good subjects for avertin narcosis.

Dosage of Avertin

The amount of avertin administered to a patient is calculated, for want of a better method, according to the body-weight. The standard dose used for attaining basal narcosis is ·1 gram per kilogram of body-weight, and there is much evidence to show that this dose should not be exceeded and certainly not by anyone who has not had considerable experience in the use of the drug.

Lewis and Edwards, as already stated, consider that a dosage calculated according to the Basal metabolic rate would be more satisfactory and in certain cases this might be necessary but, being a laborious procedure, it is obviously unsuitable for routine use.

Blomfield[34] states "Obviously mere body-weight is an insufficient guide to the correct amount of a narcotic substance to employ on the body of a patient whose mental attributes decide so largely his reaction to drugs of this kind."

This dosage by body-weight is quoted as one of the disadvantages of avertin by those who favour the barbiturates which, when administered intravenously, have a dosage regulated to the needs of each individual patient. In the writer's opinion this disadvantage is outweighed by the "barrier action" of the liver where the rectal route is employed.

Larger doses of avertin were used by some of the early workers in the effort to produce full surgical anaesthesia but it has been definitely established that, if safety is to be the first consideration, avertin must be used solely as a basal narcotic. Anaesthesia may be attained in a limited number of cases, but should not be aimed at. Killian (35) referring to this subject says "when one desires to go beyond this (i.e. sleep production), then one demands of the molecule more than it is able to perform without injuring the human organism."

In the experience of the writer, the standard dosage has given satisfactory narcosis in every case and only very occasionally has it been deemed necessary to depart from it, and then never in the direction of an increase. For very debilitated or very stout patients the obstetric dosage (·075 gram per kilogram of body-weight) has been found sufficient.

Maddox (36) advises using variations of dosage after experience has been gained in the use of the drug and also displays a tendency to aim at securing full surgical anaesthesia without the use of supplementary anaesthetics. In the writer's opinion such procedures are not only unjustifiable but unnecessary as all the psychological benefits may be obtained by the standard dose and the amount of inhalational anaesthetic usually required is so small as to have

little deleterious effect. Vomiting was exceptional and post-operative lung complications were entirely absent in his series of cases treated strictly according to the basal dosage and in no case was the patient in any danger as a result of the drug.

Premedication

The question of premedication must be considered in conjunction with posology. Morphia is the drug which is in most common use. In the writer's opinion the use of morphia prior to the exhibition of avertin is unnecessary and definitely adds to the risk. That this is the feeling among many observers will be seen by a study of the more recent writings on the subject. Young (24) originally used $\frac{1}{4}$ of a grain of morphia one hour before avertin, but being dissatisfied with the condition of his patients with that dose, now uses only $\frac{1}{8}$ of a grain. Blomfield and Shipway (5), in an early article before the general issue of the drug, recommend morphine and atropine (Blomfield), morphine and scopolamine (Shipway) or omnopon alone (Blomfield). The same two writers at a later date (37) at a discussion on avertin at the Royal Society of Medicine (Section of anaesthetics) sound a note of warning. Shipway says he omits morphia if there is likely to be a large fall in blood-pressure or much loss of blood.

Blomfield thinks morphia is unnecessary.

In Maddox technique (38) 1/6 of a grain of morphia is given threequarters of an hour before avertin. He is very insistent that the interval should not be reduced and that a larger dose should not be given. He also specifies definite types of cases in which morphia must not be used such as cases of cachexia and depleted glycogen reserve. He has not had much experience of the barbiturates but appears to think that they are preferable to morphia as a premedicament.

Both morphia and avertin have a strong depressant action on the respiratory centre, and as satisfactory narcosis can be given in the majority of cases by the use of the latter alone, it seems that the use of morphia is unnecessary except possibly in powerful alcoholics, who are notoriously resistant to any form of anaesthesia and in them the dose should not exceed 1/6 of a grain and this should be given not less than three quarters of an hour before avertin.

The oral administration of $1\frac{1}{2}$ grains of nembutal on the night previous to operation is of advantage in some very nervous patients and this drug may also be used in the same dosage as a premedicament in place of morphia.

Atropine sulphate (1/150 to 1/100 of a grain) should be given as a routine in all cases to lessen the amount of mucous in the air passages.

Other drugs which are sometimes used as pre-medicaments are the barbiturates Luminal, Dial, Phanodorm, optalidon and sodium—amytal.

As a point of general anaesthetic technique, the patient should not be starved prior to operation and it is an advantage to give copious fluids and some glucose, especially to children.

A Technique of Avertin Administration

The Bowel: A mild aperient is given on the evening prior to operation and, if this has acted satisfactorily by morning nothing further need be done, otherwise a small soap and water enema is given. Washing out the bowel is supposed to interfere with its absorptive powers and is better omitted. Emergency cases to whom neither aperient nor enema have been given have not shown any variation in the rate of absorption.

Preparation of Solution: Avertin fluid is used. The requisite amount is measured according to body-weight, the calculation being made from the chart supplied by the makers, and is added to the given quantity of distilled water heated to 40°c in a 1000 c.c. Erleu-

mayer flask. The result is a 2½% solution of avertin containing ·1 gram of the drug per kilogram of the patient's weight. After thorough shaking the solution is tested by adding two drops of 1·1000 congo red solution to 5 c.c. and if the resultant solution does not turn blue, the preparation is fit for use and may be given to the patient. A blue discoloration after the addition of congo red indicates the formation of dibromacetaldehyde. The test is obligatory in every case.

On no account must the solution be re-heated and it should be made up fresh for each case.

Administration: The prepared solution is run into the bowel by means of a funnel and catheter (No. 8), with the patient in the Sims position on his left side. He is instructed not to strain and to endeavour to retain the solution at all costs, (in the writer's series of cases none of the patients returned the solution) The catheter is lubricated and pushed into the bowel for about four inches. Usually the solution runs in easily. If any difficulty is experienced the catheter should be moved slightly. The administration generally takes about ten minutes but a greater or less period does not appear to make much difference to the result. The catheter is then removed except in the case of

perineal operations where it should be clamped and left in situ, so that the unabsorbed fluid may later be siphoned off before the operation is commenced.

As a rule the patient drops off to sleep in about 15 to 20 minutes, and the narcosis deepens for about 30 minutes after which time the patient may be given the injection of atropine and moved to the operating theatre. Very occasionally he may open his eyes and talk at this point. During the period between the induction of sleep and removal to the theatre the patient should be kept on his left side and a careful watch kept on his airway. On no account must he be left alone once narcosis has been induced.

Reflexes: These disappear in the usual manner (27) and the patient when fully narcotised has contracted pupils that react to light, absent conjunctival reflexes and absent or very slight corneal reflexes. The skin reflex may or may not be present. It cannot be too definitely stated that the condition of the eye reflexes does not give a clue to the preparedness of the patient for the commencement of operation.

At this stage the application of a mask saturated with ether will usually case alteration in respiration, coughing, or movement of the head, and is a useful test of the depth of narcosis.

Another useful test is the application of a tongue clip.

The Supplementary Anaesthetic: In the majority of cases, where a major surgical procedure is to be carried out some supplementary anaesthetic is required.

The most commonly used agent is ether and, as mentioned above, the application of a mask saturated with ether is a useful test of the depth of narcosis. If the patient is quiescent after inhaling a little ether, a tongue-clip applied will generally cause some resentment. Further administration of a small quantity of ether will produce sufficient anaesthesia for the toleration of a Hewitt's airway and at this stage the operation can be safely commenced. If there is any reaction to the incision, very little more ether will rapidly deepen the anaesthesia. Further administration of ether during operation is very easily and satisfactorily given by means of Shipway's warm ether-vapour apparatus connected to a cylinder containing 5% CO_2 and 95% oxygen. A catheter or malleable metal tube is connected to the delivery pipe of the apparatus and the vapour can thus be given by the nasal route or by introducing the metal tube into the airway. The writer finds the Shipway mask very convenient to use, the delivery tube of the apparatus being connected directly to it.

By these means warm ether vapour is conveyed

to the patient supplemented by CO_2 and oxygen which, should occasion arise, may be given pure merely by altering the tap on the apparatus. By means of the nasal catheter the anaesthetist can administer the anaesthetic and yet be some distance from the patient, a point which is of great advantage in operations on the head and neck. Less ether is required by this method than by the open method and it has the additional advantage of being warmed before it reaches the patient.

Nitrous oxide and oxygen may also be used very satisfactorily and is of special advantage in cases of lung disease and diabetes. It is also useful for raising the blood-pressure (22). Used alone, gas and oxygen is often unsatisfactory on account of poor relaxation. Avertin does away with this objection and the combination gives a very fine anaesthetic with minimal after-effects. The chief disadvantages of gas and oxygen are its importability for private work and that, unless administered by the intratracheal route, it is very tiresome to maintain over long periods.

Chloroform should never be given as a supplementary anaesthetic.

Prior to the removal of the patient from the table, it is the writer's custom to flush out the lungs with CO_2 and oxygen. This deepens the

respiration, expands the lungs, stimulates the circulation and helps to hasten the elimination of the supplementary anaesthetic. By the method just detailed, this can be done without any trouble. This procedure aids in the prevention of lung complications and is used in every case anaesthetised in the hospital, whether by avertin or other means. Since it has been in use (9 months) there has not been a single case of post-operative pneumonia. As an added protection each patient wears a gamgee chest-protector during and after operation and is carefully guarded from cold during transit from theatre to ward.

Subsequent procedures: When the patient leaves the theatre a tongue clip is left in situ (the ordinary Backhaus clip is used and, as it causes little trauma, patients seldom complain of any after pain as a result) and is removed as soon as it is resented.

On return to bed a careful watch is kept on the airway until the return of consciousness which usually takes place in from 2 to 3 hours after the administration of avertin, depending partly on the amount of supplementary anaesthetic used. Generally the patient wakens, moves his limbs and may answer questions if spoken to, and then lapses into a natural sleep which lasts for some hours.

Patients who have had markedly depressed respiration during operation or whose condition either prior to

operation, or as a result of operative procedure appears to render them specially liable to lung trouble have CO_2 and oxygen administered at intervals according to the needs of the case. For this purpose special canvas tents with cellophane windows have been constructed on the lines suggested by Randell Henderson (39).

No further treatment is given to the bowel.

Post operative restlessness: This occurs fairly frequently but is usually easily controlled by morphia given as soon as the restlessness is established. Fortunately such cases do not appear to suffer from respiratory depression and there does not seem to be any risk in giving morphia.

Additional points in Technique: The actual administration of the Avertin solution is best left to the ward-sister (or staff-nurse), provided she has been previously instructed by the anaesthetist. The presence of the anaesthetist at the bedside may alarm a nervous patient, but a rectal injection by one of the staff to whom he is accustomed carries with it no fears.

There should be available in the ward during administration the following emergency requisites:

(1) Hypodermic syringe charged with $\frac{1}{2}$ a grain of Ephedrine sulphate (or one of the other blood-pressure raising drugs already mentioned).

(2) A cylinder of CO_2 and oxygen 95%, with fine adjustment and nasal catheter attached.

(3) Tongue forceps.

(4) Some form of artificial airway (e.g. Hewitt's)

In the writer's practice none of these measures has been required as no patient exhibited any cyanosis or gave any anxiety as regards the respiration or pulse. Great care should always be taken to ensure that when sleep has been induced, the patient's head is on its side and in a comfortable position. If this is done there is seldom likely to be trouble with the airway.

Avertin in Obstetrics

General: The search for a suitable anaesthetic for relieving the pains of childbirth still goes on and many and varied are the methods in use at the present day. If a census of all practitioners in the British Isles were to be taken it is probable that the most favoured anaesthetic would still be chloroform, administered on an open mask. In other words, the majority of doctors still employ the method introduced by Simpson in 1847. The reason for this is that no more recent method has been devised which is so simple to administer and which gives such good results with comparative safety. No one, however, will deny that chloroform anaesthesia is tedious when given for long periods during the second stage of labour and that, if unskilfully administered, it will bring labour to a standstill. Again, in spite of the fact that accidents with chloroform are less

frequent in obstetrics than in surgery, it still remains a potent tissue poison and must be used with caution.

The probability is that in the majority of cases the anaesthetic is withheld until the end of the second stage, and anaesthesia à la reine is the exception rather than the rule.

Movements are on foot at the present time, both within the profession and among the lay public, to provide every mother with anaesthesia during labour and mention may be made of Carnac Rivett's method (40) of chloroform capsules, which is at present being tested in many hsopitals throughout the country, the expense being defrayed by public enterprise.

Other methods of inducing obstetrical anaesthesia or analgesia which are in use are: (1) Scopolamine-morphine narcosis ("Twilight sleep"). This method is generally held to be unsuitable for use in general practice and demands much skill and experience in order to procure satisfactory results. It has also the disadvantage that it prolongs labour and that the baby is sometimes born apnoeic. Occasionally patients treated by this method become maniacal and are exceedingly difficult to restrain.

(2) Nitrous oxide and oxygen is a satisfactory anaesthetic (41) but usually requires the presence of an anaesthetist and a cumbersome apparatus which makes it quite unsuitable for general use.

(3) Spinal and Sacral analgesia (40) are not satisfactory owing to their short duration and also because they inhibit the longitudinal muscular fibres, giving a hard uterus with little expulsive power. There is also the remote risk of persistent paralysis following the injection.

(4) Rectal Ether: This method, much used in America, has never been very popular in this country. The injection is large and is frequently expelled. It is not so satisfactory as avertin.

(5) The Barbiturates: These agents are becoming very popular and will probably become more so. The ease of administration of nembutal and chloral, with its excellent results for both mother and child make it a most satisfactory anaesthetic, especially when working single-handed.(42)

(6) Avertin: Avertin has been used extensively in labour and is probably preferable to all the methods mentioned above, with the exception of the barbiturates. Most of the literature on the subject, whilst being favourable, is not unduly enthusiastic.

Frankenstein (43) considers it inferior to pernocton, in view of its elaborate preparation and the difficulty of keeping the patient clean. Rivett (40) does not mention it! Hewer (41), whilst mentioning it, does not consider it sufficiently efficacious to have advantages over gas and oxygen. Newell (44), in a record of 100

cases, considers it preferable to oil-ether, owing to the small injection and the absence of the burning sensation in the rectum which often follows the latter method.

Morgan (45) gives a record of 45 cases satisfactorily treated with avertin and has evolved a useful technique of administration. Incidentally she does not give a preliminary injection of morphia and makes no mention of the addition of milk to the solution with a view to prolonging its action.

Connell (46) says that, though avertin increases the duration of labour, it is not by so much as is generally thought. In his series of about 50 cases the length of the second stage under avertin was 4·6 hours, and without avertin 3·7 hours. He notes that frequently the uterus in the third stage is not so firm as usual, but that this did not lead to any apparent increase in haemorrhage.

Gauss (47) says that the use of avertin in labour is not justifiable, as it gives only a short anaesthesis of $1\frac{1}{2}$ to $1\frac{3}{4}$ hours, and that the greater part of labour pains have to remain. This is hardly a fair criticism as most other writers have found the anaesthesia longer than he states, and also recommend that a second and even a third injection may be given if necessary.

Coghlan (48) says that the average number of injections necessary is three in a primipara and two

in a multipara. He uses a dosage of ·05 grams per kilogram of body weight for the second and subsequent injections and also gives magnesium sulphate and novocain as a premedicament instead of morphia. Connell, in the paper already quoted, says that, in avertin, we have something which fulfils the requirements of safety, ease of administration, absence of undue prolongation of labour, and portability. A drug which fulfils these requirements is indeed of great use, though it may not necessarily be the best available.

Avertin can be used in all normal labours, especially in primiparae, and in abnormal cases where the patient is exhausted it can still be given. This applies particularly to posterior positions of the occiput where time must be allowed to permit of anterior rotation. In any abnormal case, should operative interference be required, such as Caesarean section, avertin does not further prejudice the chances of either mother or child. With regard to Caesarean section, where spinal analgesia is the method of choice, avertin in the obstetric dosage may safely be used.

Technique of Administration of Avertin in Labour

Premedication: As soon as first stage labour pains are well-established ¼ of a grain of morphia should

be given hypodermically. This is sufficient to dull the earlier pains and to allow a quiet dilatation of the os. Morgan (45) omits any premedicament and quotes a case in which great difficulty was encountered in resuscitating a child where ¼ of a grain of morphia along with scopolamine had been given 3 hours before avertin and 6 hours before delivery. Probably morphia would be better omitted in multiparae, as in them the duration of the first stage is extremely difficult to gauge, and its use reserved for primiparae.

Preparation and Administration of the solution: The solution is prepared in the same manner as for surgical operations except that the amount used is less. The obstetric dosage is ·075 grams per kilogram of body-weight given in a 2½% solution in distilled water, the amounts being calculated from the maker's chart. The congo-red test is, as usual, obligatory. The addition of 2 ounces of milk to the solution is said to prolong the action of the drug.

The patient may be weighed either at the end of the eighth month (Morgan) or at term. If the latter, then 9 pound should be deducted for the weight of the child and placenta (Maddox).

The solution is administered with the patient in the Sim's position on her left side. A fairly stiff rubber catheter, size 10, should be used. Immediately

following a pain, the catheter is introduced into the bowel and pushed up past the head and the solution run in fairly rapidly. If a pain supervenes, then the catheter must be immediately clamped and a pad held over the anus to prevent the return of the solution. It is unnecessary to remove the catheter. When the pain passes off, the solution is again run in and so on, until the patient has received the full amount. The catheter is then removed and the anus guarded during the next few pains.

Time for Administration: In primiparae, avertin should not be given until the os is fully dilated; in multiparae it may be given at three-quarter dilatation.

Progress of Labour: After avertin the patient becomes drowsy in from 15 to 20 minutes, and may drop off to sleep. The pains continue at regular intervals and during them the patient may groan or cry out and be restless, returning to the somnolent state as soon as the pain has gone. In patients who do not sleep but remain talkative and cry out loudly during pains there is usually complete amnesia which is as gratifying as it is surprising.

Repeated doses: Occasionally one administration of avertin is not sufficient, especially in complicated labours in primiparae, and subsequent doses have to be given. The dosage in such cases should be ·05 to ·06 grams per kilogram of body-weight and a second

dose should never be given within 3 hours of the first. Supplementary anaesthetic: A patient narcotised with avertin in labour can quite safely be subjected to inhalation anaesthesia if required. Ether is probably the anaesthetic of choice, or gas and oxygen if available, but chloroform has been administered without adverse effects to either mother or child (45).

To sum up, Avertin is a very useful anaesthetic in labour. Its chief disadvantages are that its action is comparatively short and that its use calls for sound obstetric judgment in order to gauge the correct time for administration.

The writer has used it on only two occasions. Both patients were primiparae and both had posterior positions of the occiput requiring manual rotation and instrumental delivery. Amnesia was perfect in both cases and the condition of the mothers and children entirely satisfactory. The long after-sleep that ensued in both cases was striking and of great benefit. Both cases were dealt with single-handed and the supplementary anaesthetic (ether) was given by the midwife. One would have no hesitation in using avertin again under similar circumstances.

Milk was used along with the solution in both cases and in the second case gave four hours narcosis

prior to the administration of ether. The objection that avertin tends to hamper asepsis was overcome by siphoning off the remaining fluid prior to intervention.

NOTES on a Series of Seventy one cases
of Avertin Narcosis conducted by the Writer

The following series of cases was observed mainly at the Royal East Sussex Hospital, Hastings.

The writer first introduced Avertin to the Hospital in January 1932 and it is now used in the majority of cases.

This series does not represent all the avertin administrations from January to September 1932, but only those personally supervised and where the supplementary anaesthetic also was personally administered. The house surgeons, having been instructed in technique, now use Avertin in suitable cases.

The aim of the investigation was to use avertin in as large a variety of surgical conditions as possible and to note any special advantages or disadvantages in each case.

The technique used was the one already described, omitting the use of morphia.

Statistics

Seventy-one cases received Avertin as a basal narcotic; of these 27 were males and 44 were females.

The average age of the males was 25·3 years and of the females 38·3 years. The youngest male was aged 6 years and the oldest was aged 76 years. The

youngest female was aged 4 years and the oldest was aged 65 years.

Operations for which Avertin was used

(1) General Surgical Operations: 37 cases.

Amputation of breast	6 cases
Gastro-enterostomy	4 cases
Nephrectomy	4 cases
Partial thyroidectomy	4 cases
Herniotomy	3 cases
Dissection of glands of neck	3 cases
Cerebral decompression	2 cases
Laparotomy	3 cases
Cholecystectomy	2 cases
Removal of cyst of neck	1 case
Removal of lipoma of back	1 case
Operation for varicocele	1 case
Operation for osteomyelitis of jaw	1 case
Amputation of forearm	1 case
Enucleation of chondroma of finger	1 case
Total	37 cases

(2) Operations on the ear, nose and throat: 14 cases

Dissection of Tonsils	9 cases
Submucous resection of nasal septum	3 cases
Operation on mastoid antrum	2 cases
Total	14 cases

(3) Gynaecological operations: 7 cases

Sub-total hysterectomy	3 cases
Bilateral salpingo-oophorectomy	1 case
Perineorraphy	1 case
Operation for Ectopic Gestation	1 case
Dilatation and curettage	1 case
Total	7 cases

(4) Orthopaedic operations: 5 cases

Operation for Hallux valgus	4 cases
Albée's operation	1 case
Total	5 cases

(5) Ophthalmological operations: 6 cases

Operation for Strabismus	2 cases
Enucleation of eye	1 case
Stitching of conjunctiva (emergency operation)	1 case
Trephining operation for Glaucoma	1 case
Removal of large cyst of eyelid	1 case
Total	6 cases

(6) Labour: 2 cases (already mentioned)

Commentary on Cases

General: In every case narcosis was obtained. Apart from the cases mentioned later under tonsillectomy, no case gave any cause for anxiety either prior to, during or after the operation. In no case was there any

anxiety due to the use of avertin.

Post-operative vomiting was never seen on more than one occasion after operation, even in stomach cases, and in no case was there any post-operative lung complication. There were no deaths in the series and the use of the drug has met with the approval of the surgical and nursing staffs alike.

The patients were all questioned after operation as to their sensations, and were unanimous in praising the pleasantness of the induction. Those who had previously had ordinary inhalation anaesthetics were most definite in their preference for avertin and several of them expressed surprise at the absence of sickness.

In the breast and thyroid cases, the claims made for avertin, as a means of preventing psychological shock were fully substantiated. Two of the goitres were successfully "stolen." The advantage of easily controllable anaesthesia, where the anaesthetist could station himself well away from the patient, was very obvious in the head and neck cases. The depth of anaesthesia was easily gauged by observing the character of the respirations.

Abdominal operations were most satisfactory. The absence of large respiratory movements and the excellent relaxation simplified and shortened the operations and as stated above vomiting was practically absent.

Both the decompression operations were for cerebral tumours and in them very little additional anaesthetic was required. The advantage of a clear field for the surgeon was again in evidence.

In the kidney cases, which are usually difficult to anaesthetise, owing to the awkward position of the patient, anaesthesia was easily maintained. There was no noticeable difference in the recovery time of these patients.

Of the remaining general surgical operations little need be said except that in the operations for amputation of the forearm, varicocele and lipoma of the back a few drams of ether was all that was required in the way of supplementary anaesthetic.

The gynaecological cases were uniformly successful as was to be expected following the extensive experience of Young in this type of patient. The psychological factor was much appreciated.

Two of the operations for Hallux valgus were performed without any additional anaesthetic. The Albee's operation was interesting on account of the prone position of the patient, and in it anaesthesia was smooth and uneventful, whereas it would have been difficult and tedious under the older method.

Very little has been written about the use of Avertin in ophthalmology as most of the operations in this branch of surgery are performed under local anaesthesia. It is,

however, in the very nervous patient that a general anaesthetic is sometimes required and avertin was most suitable in the cases undertaken.

All the operations passed off uneventfully and the ophthalmic surgeon now demands the use of avertin whenever he finds it necessary to employ a general anaesthetic.

The case of Enucleation of the eye was of particular interest as the patient was an old man of 76, suffering from marked myocardial degeneration and arterio-selerosis, and was definitely a bad risk for anaesthesia. As the operation was urgent and essential it was thought justifiable to use avertin and the procedure was eminently successful. The patient recovered well, though he was restless for about an hour and refused to believe that he had had his operation!

Submucous resection of the nasal septum was easily performed under avertin. A post-nasal plug was inserted and ether, CO_2 and oxygen were administered via a Hewitt's airway. The mastoid operations, one of them on a child of four years, were also successfully performed and the prolonged after-sleep was of great benefit.

After the first few tonsil dissections the general opinion was that a satisfactory method of anaesthesia for these difficult cases had at last been found, but two later cases caused an alteration of this view. The trouble arose in both cases through the disappearance of the laryngeal reflex. In the first case this happened

suddenly, - she had coughed successfully a few breaths previously - and a blood clot apparently got into the larynx and despite the surgeon's efforts at removal could only be got rid of by investing the patient. Her subsequent progress was uneventful as the reflex quickly reappeared after liberal use of CO_2 and oxygen.

The second case, also a woman, had re-established both pharyngeal and laryngeal reflexes before leaving the table but on return to the ward they again disappeared and remained absent for three hours, during which time the house surgeon was in constant attendance removing blood-clot from the pharynx. Neither case had had more supplementary anaesthetic than usual, and there was no indication whatever that the reflexes were liable to disappear. The second case was more alarming, as the possibility of a reflex disappearing once it has been re-established is a very grave one.

The problem of anaesthesia for tonsillectomy is a very real one and has been the subject of much correspondence in the Lancet during recent months. Opinions among the surgeons differ as to what is the best condition of the throat reflexes. Some demand their abolition during operation, others demand that they should be present throughout.

For ease of working avertin gives a perfect anaesthesia, but apparently there is the occasional case which will suddenly and without warning lose

its reflexes for a time and on this account the use of the drug for this operation is unjustifiable.

A technique which would render the use of avertin safe for tonsillectomy would be one where the rubber intra-tracheal tube with inflatable rubber cuff devised by Guedel and Waters (49) was used. The tube could be left in situ until resented by the patient, by which time all danger would be past.

The writer, therefore, does not now use avertin for operations on the tonsils but prefers to use numbutal, as a premedicament, without morphia.

It will be noted that the series of cases here detailed is representative of most types of case encountered in a general hospital of medium size. The only cases that were not considered suitable for avertin were cases of prostatic enlargement with marked renal insufficiency. In order that such cases might have the benefit of basal narcosis, they were given 3 grains of nembutal and $\frac{1}{4}$ of a grain of morphia one hour before operation and spinal analgesia was produced by Stovaine. Sleep was not produced by this means so satisfactorily as in avertin narcosis, but the spinal injection was tolerated without demur and with the aid of a little gas and oxygen at the commencement of the operation the patients slept peacefully throughout. Four cases were treated in this manner.

Conclusions

(1) Every patient about to undergo a surgical operation should have the benefit of basal narcosis in some shape or form.

(2) At the present time Avertin is the most satisfactory and generally applicable basal narcotic available.

(3) Avertin is invariably safe if a dosage of ·1 gram per kilogram of bodyweight be not exceeded.

(4) Morphia should not be used as a premedicament as it is unnecessary and adds to the risk.

(5) Avertin is essentially a basal narcotic and not a general anaesthetic.

(6) The supplementary anaesthetic is of great importance in obtaining successful after-results and a simple technique for its administration is detailed. Emphasis is laid on the use of CO_2 and oxygen after operation.

(7) Avertin may be used with advantage in obstetrics but it is probably inferior to nembutal and chloral as a routine anaesthetic, especially where working single-handed.

(8) Practically every surgical condition can be dealt with under avertin. The contra-indications to its use are according to the condition of the patient rather than to the procedure to be adopted, with the exception of operations on the anus and rectum, and tonsillectomy.

(9) Tonsillectomy should not be performed under avertin unless a special technique is adopted.

(10) Certain conditions of the patient are better treated by avertin than by other means. These are cases of thyroid disease, diabetes, heart cases and all patients of a particularly nervous temperaument.

(11) There is a definite field for the use of avertin in ophthalmology.

(12) In the foregoing series of cases the results of Avertin narcosis were uniformly satisfactory (with the exception of the two tonsil cases mentioned above) and post-operative complications were conspicuous by their absence.

Though the series is small it covers many different varieties of surgical procedure and the results obtained have been so successful as to warrant the continued use of the drug.

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